REMARKS

Claims 27-31 and 34-35 were pending in the present application. Claims 1-26 and 32-33 had previously been canceled without prejudice. Claims 28 and 34-35 have been presently canceled, without prejudice, claims 27 and 29-31 have been amended and new claims 36-56 have been added. Accordingly, claims 27, 29-31 and 36-56 will be pending upon entry of the instant amendment. Any amendment or cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite prosecution of the application. No new matter has been added by virtue of the amendments. Support for the new claims can be found in the original claim set, as well as, for example, page 28, beginning at line 22, at page 44, beginning at line 7, at page 58, beginning at line 5, at page 59, beginning at line 22, at page 63 beginning at line14, at page 65, beginning at line 15, and at page 67, beginning at line 3.

The Rejection of Claims 27-31 and 34-35 under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 27-31 and 34-35 were rejected under 35 U.S.C. § 112, second paragraph, for reciting the limitation "wherein the test compound is useful for modulating the phenomenon". Specifically, the Examiner states "there is insufficient antecedent basis for the term 'phenomenon' in the claim."

In the interest of expediting prosecution, Applicants have canceled claims 28 and 34-35 and amended claims 27 and 31 to remove reference to the term "phenomenon." Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, second paragraph rejection.

Claims 27-31 and 34-35 were additionally rejected under 35 U.S.C. § 112, second paragraph, as "being incomplete for omitting essential steps". Specifically, the Examiner states that the omitted step is "establishing that the compounds identified in the present methods that modulate 47169 activity also modulate tumorigenesis."

Applicants respectfully traverse this rejection, however, in the interest of expediting prosecution, and without acquiescing to the Examiner's rejection, Applicants have canceled

claims 28 and 34-35 and have amended claims 27 and 31 to recite: " ....b) comparing the ability of the compound to modulate tumorigenesis in the first composition as compared to a second composition that is substantially identical to the first composition, except that it lacks the compound, whereby the difference in the ability of the compound to modulate tumorigenesis in the first composition as compared to the second composition is an indication that the compound is useful for modulating tumorigenesis; and c) selecting a compound capable of modulating tumorigenesis; thereby assessing whether a compound is useful for modulating tumorigenesis." These claims now establish that the candidate compound(s) identified to modulate the glycosyl transferase activity also modulate tumorigenesis. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, second paragraph rejection.

The Rejection of Claims 27-31 and 34-35 under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

Claims 27-31 and 34-35 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Applicants have canceled claims 28 and 34-35 and amended claim 27. Claim 27 and new claim 43 recite: 1) that the polypeptide be encoded by a nucleic acid molecule at least 95% identical to SEQ ID NOs:1 or 3; 2) that the polypeptide be at least 95% identical to the polypeptide of SEQ ID NO:2; or 3) that the polypeptide comprises a fragment of at least 100 contiguous amino acids of SEQ ID NO:2; and that such polypeptides each exhibit glycosyl transferase activity.

In light of these presently pending claims, Applicants traverse the Examiner's rejection and argue that they were in possession of the claimed invention at the time of filing for the reasons discussed below.

Applicants have taught that biologically active portions used in the claimed invention may include sequences of at least 100 contiguous amino acids of SEQ ID NO:2 (see *e.g.* page 28, beginning at line 22). Likewise, Applicants have additionally taught that isolated polypeptide molecules used in the invention include polypeptide sequences which are at least 95%, or more homologous to the entire length of the polypeptide sequence shown in SEQ ID NO:2 (see *e.g.* page 44, beginning at line 7).

Applicants have taught domains within the 47169 polypeptide which are conserved and essential for activity of the polypeptide, namely the glycosyl transferase 2 domain and ricin lectin domain (see *e.g.* page 10, beginning at line 19). Having identified regions necessary for activity, Applicants have taught which regions of the polypeptide are amenable to alterations as well as those which are not amenable to alterations. For example, Applicants teach at lines 18-21 on page 27 that "amino acid residues that are conserved among the polypeptides of the present invention, e.g., those present in the glycosyl transferase 1 and glycosyl transferase 2 domains (i.e., hereafter collectively referred to as a glycosyl transferase domain) and ricin lectin domains are predicted to be particularly non-amenable to alteration." Applicants have also provided an example of a specific fragment comprising at least 100 contiguous amino acids of SEQ ID NO:2 which exhibits the glycosyl transferase activity, namely the glycosyl transferase 2 domain located at about residues 148-333 of SEQ ID NO:2 (see *e.g.* page 10).

Additionally, the specification teaches one how to generate functional variants by performing conservative substitutions within the polypeptide used in the claimed invention. As defined at page 27 beginning at line 22, "A 'conservative amino acid substitution' is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain." The Applicants have also defined which of the amino acids have similar side chains, thereby providing a skilled artisan the necessary tools to generate functional variants of the polypeptide used in the claimed invention.

Finally, Applicants have provided teachings for one of skill in the art to be able to perform assays to determine whether or not specific sequences have the desired glycosyl transferase activity. For example, as taught on page 22-23 of the specification, a 47169 protein can have one of the following activities: "(1) catalyzing formation of a covalent bond between a carbohydrate (i.e., saccharide) moiety and a hydroxyl or amino moiety of a protein (e.g., a serine, threonine, or tyrosine side chain of an amino acid residue of a protein) or lipid; (2) facilitating non-covalent binding between a protein and a cell, virus, or other protein; (3) modulating cell signaling; (4) modulating cell differentiation; (5) modulating tumorigenesis; (6) modulating cell adhesion; (7) modulating cell motility; (8) modulating a cell-to-cell interaction; (9) modulating cell invasivity (e.g., metastatic or extravasative capacity of an individual cell or invasion of surrounding tissues by a tumor); (10) modulating cell proliferation (e.g., proliferation of breast, lung, liver, or colon tumor cells or proliferation of vascular endothelial cells); (11) modulating gene transcription; and (12) modulating an immune response (e.g., an autoimmune response or a

response to a pathogen)" among others. Based on these activities, one can perform assays on specific sequences to determine whether or not such sequences have the desired biological activities. Such assays include, for example, 1) assays which monitor the enzymatic activity of the 47169 protein or 2) assays which monitor cell growth. Performing such assays to determine whether or not a fragment or a variant of the sequence used in the claimed invention has the desired properties is common in the art and would not constitute undue experimentation.

Therefore, by having provided the full length sequence of the polypeptide used in the claimed invention, a fragment having the desired activity and an enabling disclosure for obtaining other such functional sequences, Applicants have provided the necessary teachings to demonstrate that they were in possession of the claimed invention at the time of filing. Applicants, therefore, respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection.

Claims 27-31 and 34-35 were additionally rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for failing to provide "teaching of how any function of 47169 activity is responsible for or causes tumorigenesis" Applicants were "not considered to be in possession of the methods of modulating tumorigenesis comprising comprising [sic] screening for modulators of 47169 activity."

In addition, Claims 27-31 and 34-35 were also rejected under 35 U.S.C. § 112, first paragraph, as "failing to comply with the enablement requirement." Specifically, the Examiner states that the "specification as filed does not provide sufficient guidance or appropriate examples that would enable a skilled artisan to screen for modulators of tumorigenesis using the methodology described." The Examiner asserts that the claimed methods are not enabled because 1) the method would only find inhibitors of 47169 activity and 2) the inhibitors of 47169 activity may not inhibit tumorigenesis.

Applicants respectfully traverse. Applicants have canceled claims 28 and 34-35 and amended claims 27 and 29-31. Amended claims 27 and 31 now recite:1) that a *candidate* compound be tested to determine if it has the abitity to modulate tumorigenesis in a first composition comprising the polypeptide as compared to a second composition comprising the polypeptide but not containing the candidate compound; and 2) that the compound(s) found to be capable of modulating tumorigenesis be selected. In addition, new claims 43 and 48 recite: 1) that the *candidate* compound being tested and the composition comprising the polypeptide be

combined under conditions suitable for binding; 2) that the ability of the compound to bind to the polypeptide be assessed; and 3) that a compound capable of binding to the polypeptide be selected.

In light of these presently pending claims, Applicants submit the specification provides all of the necessary teachings to enable one of skill in the art to carry out the claimed invention for the reasons discussed below.

Applicants have taught that compounds, or candidate compounds, such as, for example, small molecules and peptides, can be screened using various types of assays in order to identify compounds which bind to or modulate the activity of the polypeptide of the invention or a fragment thereof (see, for example, page 58, beginning at line 5). The teachings of the specification include, for example, cell based assays in which a polypeptide, or fragment thereof, is contacted with a test compound and the ability of the test compound to bind to the polypeptide or the ability of the test compound to modulate the activity of the polypeptide are assessed. Likewise, Applicants have also taught cell-free assays, in which soluble and/or membrane bound forms of isolated polypeptides or fragments thereof may be used for the identification of compounds that have the ability to bind to the polypeptide or the ability to modulate the activity of the polypeptide. As taught by Applicants, assessing the ability of the test compound to bind to the polypeptide or assessing the ability of the test compound to modulate the glycosyl transferase activity of the polypeptide can be achieved by a number of ways, such as, for example, the coupling of a test compound with a label, such as a radiolabel or an enzymatic label. Once labeled, an assay may be configured either to detect the label or to determine enzymatic activity (i.e. conversion of substrate to product) in order to determine if binding has occurred or if the compound has the ability to modulate the activity of the polypeptide. Applicants have additionally taught methods of performing assays without labeling any of the components of the assay by using, for example, a microphysiometer, surface plasmon resonance (SPR) or real-time biomolecular interaction analysis (see *e.g.* page 61, beginning at line 21). Additionally, the assays taught by Applicants may be performed in solution or by immobilizing the test compound or the composition comprising the polypeptide of the invention to a solid support (see *e.g.* page 62, beginning at line 1).

Applicants have therefore provided sufficient teachings and exemplification for assays which are commensurate in scope with the presently pending claims. The steps recited in the

claims would enable one of skill in the art to identify candidate compounds for modulating tumorigenesis, as only those candidate compounds which are assessed as being capable of modulating the activity of the polypeptide, or a fragment thereof, or binding to the polypeptide or fragment thereof are selected. If no candidate compound successfully modulates the activity of or binds to the polypeptide, then no candidate compound will be selected.

In addition, it is known that increased expression of a polypeptide of the invention in a diseased tissue or cell as compared to the level of expression of the polypeptide under normal physiological conditions is indicative that the polypeptide either is involved in the regulation of the disease phenomena or is responding to the disease state. Regardless of the mechanism in which the polypeptide is involved, if one of skill in the art is able to identify candidate compounds which have been selected based on their ability to bind to a polypeptide, such candidate compounds may be capable of modulating a tumorigenesis by either 1) increasing the polypeptide's activity (which may be useful if the polypeptide is responding to the disease state); or 2) decreasing the polypeptide's activity (which may be useful if the polypeptide is involved in the regulation of tumorigenesis).

In light of the teachings and exemplification provided in the present application, one of skill in the art could carry out the claimed methods without undue experimentation. Therefore, contrary to the Examiner's assertions, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of amended claims 27 and 29-31 and newly added claims 36-56. Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection.

CONCLUSIONS

In view of the amendments and remarks made herein, Applicants respectfully submit that the rejections presented by the Examiner are now overcome and that this application is now in condition for allowance. Early notice to this effect is solicited. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

This paper is being filed timely as a request for a two month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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